TRIANGULATING CORTICAL FUNCTIONAL NETWORKS WITH ANATOMICAL LANDMARKS

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ABSTRACT

Defining precisely the position of active regions obtained from functional neuroimaging studies is challenging due to the functional and anatomical variability across subjects. Traditional volumetric normalization techniques ignore the geometry of the cortex and use a relatively imprecise three-dimensional coordinate system. In this study we propose an alternative method that relates the position of functional regions on the cortical surface to the positions of the main macro-anatomical structures, the sulci. Our approach consists of using the nearest sulci to build a local referential in which the position of a region is defined. This triangulation approach improves the localization of brain regions involved in various cognitive tasks.

Index Terms— Cortical sulci, functional landmarks, surface analysis.

1. INTRODUCTION

Inter-subject variability is a prominent aspect in functional neuroimaging group studies [1]. While part of it is attributable to contextual aspects (tiredness, attention, motion and non cognitive physiological fluctuations, e.g. cardiac and respiratory rhythms) or to behavioural aspects, some of this variability might be related to anatomical differences between the subjects [2]. The standard approach consists in matching anatomical image onto a template by a non-rigid transformation (normalization) [3]. This approach is blind to the inter-subject variability in the cortical folding pattern, and thus yields only approximate anatomical correspondences across subjects.

Although it has been suggested that surface-based cortical mapping may be more precise than volume-based brain mapping [4], a quantitative analysis of this approach is still lacking. In this work, we propose to define the position of regions found in functional neuroimaging protocols based on anatomical features extracted individually. On the cortical surface, the sulci represent the main landmarks to define the position of the regions [5]. More specifically, we propose to use the geodesic distance between target points on the cortical surface and their neighboring sulci to define their position. For instance, in general any point on the cortical surface is uniquely defined by its distance to the three nearest sulci, and we use explicitly this *triangulation* principle to define the position of a region across subjects.

In order to test the validity of this approach, we *i)* use some functional landmark (FL) regions, which are reproducible foci of activity in a given group of subjects, *ii)* measure the variability of the position of these FLs when the data is analysed in the standard space and then projected onto the individual cortical surface and *iii)* compare this with the spatial variability obtained with our triangulation framework. Using cross-validation techniques, we show that the triangulation framework allows in some cases a more precise localization of some functional regions. We discuss the implications and the limits of this approach.

2. MATERIALS

$S = 31$ subjects were acquired with the 1.5T GE MRI scanner in SHFJ in Orsay-France with a localizer protocol [6]. It identifies the functional networks related to the following tasks: (i) motor (left and right hand), (ii) low-level vision, (iii) computation and (iv) reading and listening sentences. The acquisition of one dataset lasts 5 min, and comprises 128 volumes. Those data are corrected from the EPI distortions.

2.1. Functional data processing

For all subjects a standard preprocessing (distortion correction, correction of differences in slice timing, motion correction, affine normalization by coregistration to the MNI template) was performed using the SPM5 software. In each dataset a GLM analysis was then carried out to obtain a task related activity map for each condition. For a given subject $s \in \{1, ..., S\}$, let Y^s be the dataset written as matrix (scans x voxels), and let X be the design matrix that describes effects of interest and confounds; the GLM proceeds by estimating

the effect vector β^s such that

$$Y^s = X\beta^s + \epsilon^s, \forall s \in \{1, ..., S\}$$

where ϵ^s represents the residuals of the model. The estimation is based on a maximum-likelihood approach performed in each voxel, where the noise is assumed to be an AR(1) process. Let c be the linear combination of the experimental conditions that is of particular interest; c is also called a functional contrast. A certain statistic ϕ^s can be computed in each subject s to assess the presence of a positive effect $c^T\beta^s > 0$ in each voxel v of the dataset, e.g.

$$\phi^s(v) = \frac{\mathbb{E}(c^T\beta^s(v)|Y^s)}{\sqrt{var(c^T\beta^s(v)|Y^s)}}. \quad (1)$$

2.2. Anatomical data

Based on the T1 image of the brain of each subject, the Brainvisa package was used to segment different anatomical compartments (hemispheres, white matter, grey matter, cerebellum), providing white and grey matter mesh, and segmenting and labelling the sulci [5]. To label the sulci, automatic classification methods were used to extrapolate labels from the manually constructed database [5, 7]. This sequence of treatments was applied systematically to all available brains and the quality of resulting segmentation was checked. In particular, for all selected subjects the labelling was checked and in some cases corrected to solve inter-subject inconsistencies. Finally, the localization of the sulci fundi was projected onto the grey-white matter interface in each subject.

3. METHODS

3.1. Definition of functional landmarks

In order to test the validity of the triangulation approach, we need some target regions which are assumed to be analogous across subjects, and thus are likely to be located at the same position. To obtain these foci, we use the Functional Landmarks approach detailed in [1]. Basically, this approach defines in the normalized space (the MNI space) the position of the local maxima of the maps ϕ^s (see Eq. 1) for a functional contrast of interest. Those maxima which are found at reasonably similar locations in a significant proportion of subjects are then identified as a functional landmark, and possible ambiguities between multiple neighboring maxima are solved with a graph matching approach. This techniques thus provides the positions $(x_i^s)_{i=1..I}$ of I putatively analogous functional regions in a subset $\mathcal{S}(i)$ of the original S subjects.

3.2. Localizing functional regions on the cortical surface

Let $\mathcal{P}^s(.)$ be the function that projects any point of the MNI space onto the cortical surface of the subject s using a nearest-node approach.

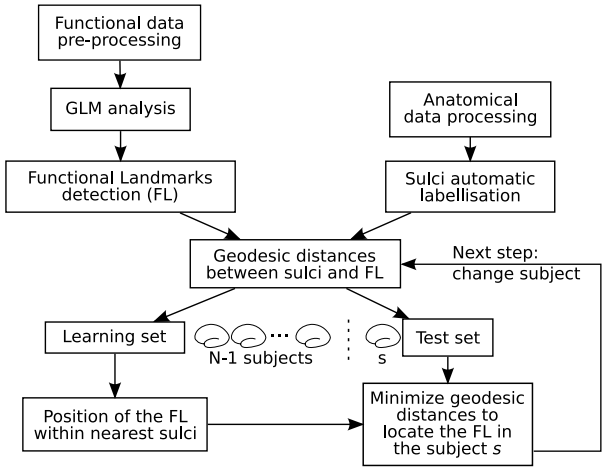

Fig. 1. Flowchart of our method. The input consists of activation images and labelled sulci. The main part of this algorithm cross-validates using leave one out method, minimizing distances to nearest sulci.

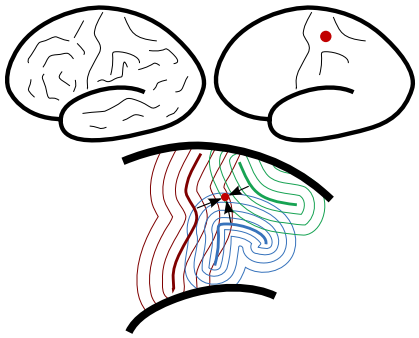

Fig. 2. The position of the functional landmark (red circle) is defined by triangulation, as the minimum of criterion defined in Eq. (2).

Note that the projection is a crucial step, which is problematic in general, given that the EPI images used to obtain functional landmarks are distorted with respect to the anatomy. In this study, the EPI images were corrected to reduce the distortions, but the correction may not be perfect, and a slight bias in the 3D space can have a dramatic effect when projecting the data onto the cortical surface, e.g. projecting a FL onto a wrong gyrus. Let $\gamma_i^s = \mathcal{P}^s(x_i^s)$ be the projection of (x_i^s) onto the grey-white matter interface. The three nearest sulcal lines on the surface around γ_i^s are identified. Let $\Gamma_i(1), .., \Gamma_i(3)$ be these sulci. Note that they are chosen at the group level, and are thus the same across subjects, even if another sulcus is closer in one of the subjects.

We propose to characterize γ_i^s by its geodesic distance to the nearest sulci, $d_{ij}^s = d(\gamma_i^s, \Gamma_i(j))$. We check the worthiness of this characterization which we call *triangulation*,

using cross-validation: let

$$\begin{aligned}\overline{d_{ij}^s} &= mean_{\sigma\in\mathcal{S}(i)-\{s\}} d_{ij}^\sigma \\ \widetilde{d_{ij}^s} &= \sqrt{var_{\sigma\in\mathcal{S}(i)-\{s\}} d_{ij}^\sigma}\end{aligned}$$

be the mean value and the standard deviation of d_{ij}^s in all subjects but s. Finally, let $\widehat{\gamma_i^s}$ be the point of the cortical surface of subject s which minimizes

$$\mathcal{J}^s(\gamma) = \sum_{j=1}^{3} \frac{(d(\gamma, \Gamma_i(j)) - \overline{d_{ij}^s})^2}{\widetilde{d_{ij}^s}^2}. \quad (2)$$

The steps performed to obtain $\widehat{\gamma_i^s}$ are summarized in Figs. 1 and 2. The minimization of the citerion (2) is performed by simple gradient descent. If the local referential is adequate, $\widehat{\gamma_i^s}$ should be very close to the actual functional landmark γ_i^s. We measure the discrepancy by the geodesic distance between the two points, $\mathcal{D}_i^s = d(\gamma_i^s, \widehat{\gamma_i^s})$. $\mathcal{D}_i^s$ represents the functional variability within the local referential based on the sulci.

To assess the quality of this method, we compare it with a volume-based approach: let $\overline{x_i^s} = \frac{\sum_{\sigma\in\mathcal{S}(i)-\{s\}} x_i^\sigma}{|\mathcal{S}(i)|-1}$ be the average position of the functional landmark i in MNI space, excluding subject s; We consider its projection on the cortical surface of the subject s: $\overline{\gamma_i^s} = \mathcal{P}^s(\overline{x_i^s})$. The quality of the standard normalization procedure is then defined as $\Delta_i^s = d(\gamma_i^s, \overline{\gamma_i^s})$. In the next section, we compare the distributions of $(\mathcal{D}_i^s)$ and (Δ_i^s) for several functional landmarks.

4. RESULTS AND DISCUSSION

Three functional landmarks were investigated (sulci names are in accordance with Ono's atlas [7]):
(i) The first landmark (represented by index (1) in Fig. 5) which corresponds to a reading activation, is located near the descending terminal ramus of the posterior ramus of the sylvian fissure, and referenced by the primary intermediate sulcus and the Superior Temporal Sulcus. This landmark could be identified in 16 subjects in the database.
(ii) The second landmark (represented by index (2) in Fig. 5) corresponds to a computation task and is located in the IPS (parietal lobe) and referenced by the ascending terminal ramus of the posterior ramus of the sylvian fissure, the inferior precentral sulcus and the main intraparietal sulcus. This landmark could be identified in 20 subjects in the database.
(iii) The third landmark (represented by index (3) in Fig. 5) also corresponds to computation and is located in the Frontal Eye Field (FEF, PreCentral lobe). It is located at the intersection of three sulci: superior frontal sulcus, marginal precentral sulcus, superior precentral sulcus. This landmark was found in 22 subjects in the database.
The box-plots of the distribution of (Δ_i^s) and $(\mathcal{D}_i^s)$ are given in the first and second column of Fig. 4 respectively. In the three cases the values of $(\mathcal{D}_i^s)$ are lower than those of (Δ_i^s) on average. Student t-test shows that the effect is almost significant in the first case ($p < 0.052$), and significant in the other cases ($p < 0.048$ and $p < 0.009$ respectively).

Our results show that a local referential can improve the accuracy of the position of some functional regions on the cortical surface. It is important to note that the detection of functional landmarks is done in the normalized space; thus our procedure to compare both referentials might be slightly biased in favor of the volume-based position definition technique. If this is the case, our results are conservative.

Our approach, as any surface-based brain mapping technique, is rather sensitive to anatomo-functional distortions that may remain after distortion corrections and anatomo-functional coregistration. This may explain why the distances (Δ_i^s) and $(\mathcal{D}_i^s)$ remain quite high in some -rare- cases (up to 30-40 mm on the cortical surface, see Fig. 4).

It is also crucial that a coherent labelling system is applied to all subjects. Errors in anatomical segmentation of the cortical surface can result in wrong identification of some sulci and therefore introduce bias in the interpretation. This bias may be significant for the whole database if the number of subjects is small.

It is important to note that the characterization of functional regions by their distances to several neighboring sulci is not the only approach for anatomical landmark-based brain mapping. In particular, for some brain regions just one or two sulci may be found near functional landmarks, in which case the present method cannot be applied. In this kind of case, e.g. close to the central sulcus or the superior temporal sulcus, it might be more adapted to use a local coordinate system along the sulcus.

In some brain regions, e.g. the frontal cortex, the identification of nearest sulci may be difficult. If the form of a sulcus is strongly variable between subjects, it can not be used as a reference. Moreover, several sulci are discontinuous, have several branches or a complex geometric form. Deciding which sulci are more reliable for functional brain mapping is an important topic for future research.

Importantly, sulcal variability is not necessarily a confound; it may also convey important information to describe different sub-populations in a group of subjects. Understanding how functional and anatomical regions jointly characterize such sub-populations is thus an important matter for the future.

When local coordinate systems cannot be used, there remains the possibility of using more global coordinate systems [4, 8]. The comparison of local and global referential for the cortical surface will be an important topic for future research. Using sulci-based referential remain in general more complex than traditional normalization techniques. On the other hand,

it may be more helpful to describe and define precisely some brain regions. Finally, it might be possible that some functional regions cannot be reliably associated with anatomical landmarks. This is an interesting question, which deserves a more systematic assessment.

5. CONCLUSION AND FUTURE WORK

We have shown that the position of some anatomical landmarks can be used to improve the localization of functional activity, by assessing the inter-subject variability of some functional landmarks. Our results imply that it would be useful to include surface-based information in brain normalization procedures. This is particularly obvious in the case of surface-based brain mapping.
A straightforward extension of this work will be to define the functional landmarks on the cortical surface directly, thus using surface-based referential instead of the MNI space [1]. Finally it remains to be decided whether local referentials are more accurate than global surface-based coordinate systems or not.

6. REFERENCES

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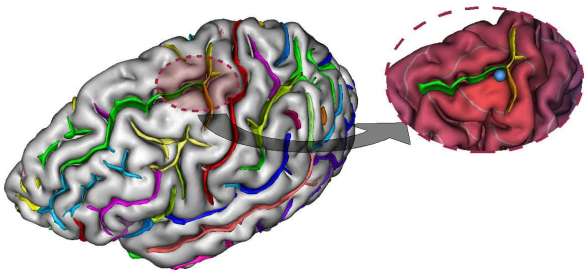

Fig. 3. Within labelled sulci framework, the activation landmark of computation (blue ball on the picture) in the prefrontal lobe is localized near the intersection of the three sulci: superior precentral, marginal precentral and superior frontal.

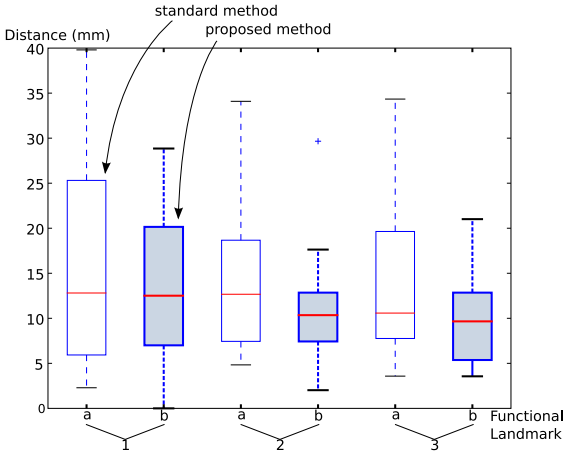

Fig. 4. Box-plot of the distances (Δ_i^s) (a) and $(\mathcal{D}_i^s)$ (b) across subjects. These results correspond to three FLs: (1) reading, (2) computation in parietal lobe and (3) computation in Frontal Eye Field.

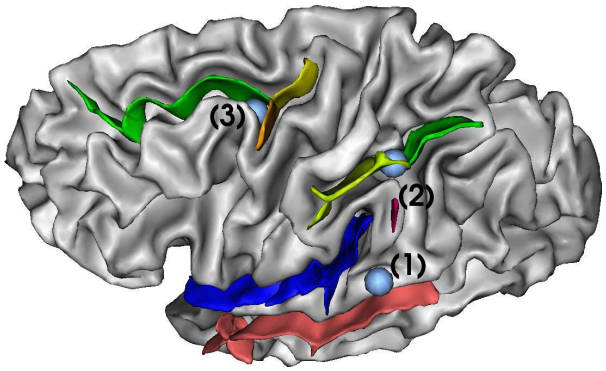

Fig. 5. The three balls on the picture represent the three functional landmarks. Each ball (landmark) is localized by the three nearest sulci.